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* * * * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 09:27:58 ON 04 APR 2007

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COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         0.21       0.21

FILE 'REGISTRY' ENTERED AT 09:28:28 ON 04 APR 2007
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L1      STRUCTURE UPLOADED

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L1                STR
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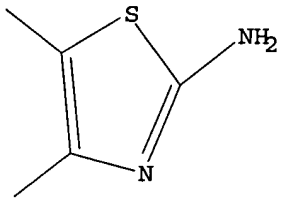


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Structure attributes must be viewed using STN Express query preparation.


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SAMPLE SCREEN SEARCH COMPLETED -      188 TO ITERATE

100.0% PROCESSED      188 ITERATIONS                                1 ANSWERS
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FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
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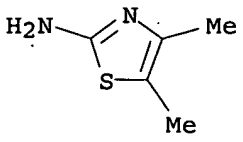

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	69.05	69.26

FILE 'CAPLUS' ENTERED AT 09:31:04 ON 04 APR 2007
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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FILE COVERS 1907 - 4 Apr 2007 VOL 146 ISS 15
FILE LAST UPDATED: 3 Apr 2007 (20070403/ED)

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They are available for your review at:

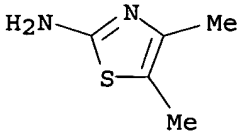
http://www.cas.org/infopolicy.html

=> s l3
L4 184 L3

=> d ti au abs so py 1-10

L4 ANSWER 1 OF 184 CAPLUS COPYRIGHT 2007 ACS on STN
TI Preparation of pyrimidyl-thiophene derivatives as Aurora kinase inhibitors
IN Adams, Jerry Leroy; Drewry, David Harold; Linn, James Andrew
GI

L5 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2007 ACS on STN
RN 2289-75-0 REGISTRY
ED Entered STN: 16 Nov 1984
CN 2-Thiazolamine, 4,5-dimethyl- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Thiazole, 2-amino-4,5-dimethyl- (6CI, 7CI, 8CI)
OTHER NAMES:
CN 2-Amino-4,5-dimethylthiazole
CN 4,5-Dimethyl-2-thiazolamine
MF C5 H8 N2 S
CI COM
LC STN Files: BEILSTEIN*, CA, CAOLD, CAPLUS, CASREACT, CHEMCATS, CHEMINFORMRX, CIN, CSCHEM, IFICDB, IFIPAT, IFIUDB, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

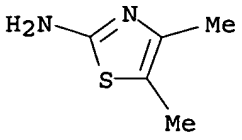
140 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
140 REFERENCES IN FILE CAPLUS (1907 TO DATE)
10 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

PROJECTED ITERATIONS: 2938 TO 4582
PROJECTED ANSWERS: 1 TO 80

L2 1 SEA FAM SAM L1

=> d scan

L2 1 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN
IN 2-Thiazolamine, 4,5-dimethyl- (9CI)
MF C5 H8 N2 S
CI COM



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

ALL ANSWERS HAVE BEEN SCANNED

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FULL SCREEN SEARCH COMPLETED - 3709 TO ITERATE

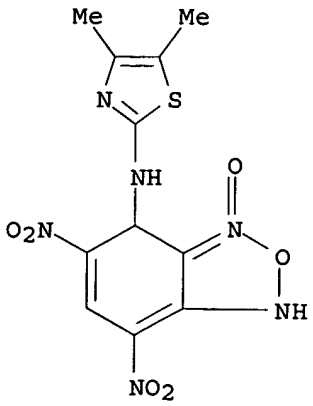
100.0% PROCESSED 3709 ITERATIONS 10 ANSWERS
SEARCH TIME: 00.00.01

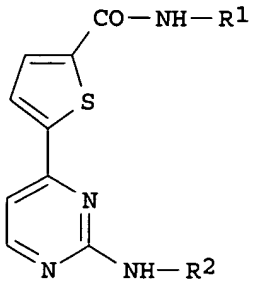
L3 10 SEA FAM FUL L1

=> d scan

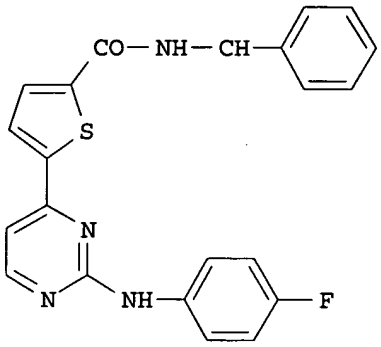
L3 10 ANSWERS REGISTRY COPYRIGHT 2007 ACS on STN
IN 2,1,3-Benzoxadiazol-4-amine, N-(4,5-dimethyl-2-thiazolyl)-1,4-dihydro-5,7-dinitro-, 3-oxide, compd. with 4,5-dimethyl-2-thiazolamine (1:1) (9CI)
MF C11 H10 N6 O6 S . C5 H8 N2 S

CM 1





I



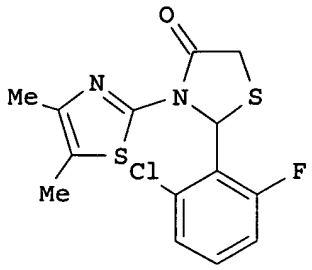
II

AB Title compds. I [R1 = HO(CH2)4-, NCCH2-, (un)substituted Ph, phenylalkyl, etc.; R2 = 2-(N,N-dimethylaminoethyl)-1,3-dioxo-2H-isoindol-5-yl, 2-(N,N-dimethylaminomethyl)-benzoxazol-6-yl, or substituted phenyl], and their pharmaceutically acceptable salts, are prepared and disclosed as Aurora kinase inhibitors. Thus, e.g., II was prepared by cyclocondensation of 5-[(2E)-3-(dimethylamino)-2-propenoyl]-N-(phenylmethyl)-2-thiophenecaboxamide (preparation given) with 1-(4-fluorophenyl)guanidine carbonate. I were tested for their Aurora kinase inhibitory activity and demonstrated pIC50 values ≥ 5.0. I as inhibitors of Aurora kinase activity should prove useful for the treatment and prevention of diseases associated with cell proliferation such as cancer.
SO PCT Int. Appl., 205pp.
CODEN: PIXXD2
PY 2007

L4 ANSWER 2 OF 184 CAPLUS COPYRIGHT 2007 ACS on STN
TI 2-Amino-5-aminomethylphenol derivatives for dyeing hair fibers
IN Pasquier, Cecile; Tinguely, Eric; Buclin, Veronique; Braun, Hans-Juergen
AB The object of the present patent application are new 2-amino-5-aminomethylphenol derivs. and colorants for oxidative dyeing of keratin fibers, particularly human hair, containing at least 1 2-amino-5-aminomethyl-phenol derivative or a water-soluble salt thereof. A 2-amino-5-aminomethylphenol derivative was prepared and used 0.00125 mol along with a developer in a hair dye formulation.
SO Eur. Pat. Appl., 28pp.
CODEN: EPXXDW
PY 2007
2007
2007

L4 ANSWER 3 OF 184 CAPLUS COPYRIGHT 2007 ACS on STN
TI Design, synthesis, and evaluation of 2-aryl-3-heteroaryl-1,3-thiazolidin-4-ones as anti-HIV agents
AU Rawal, Ravindra K.; Tripathi, Rajkamal; Katti, S. B.; Pannecouque, Christophe; De Clercq, Erik

GI



I

AB Compds. having isothiourea or thiourea functional group have shown high anti-HIV-1 activity. Therefore, a series of 2-aryl-3-heteroaryl-1,3-thiazolidin-4-ones were designed, synthesized, and evaluated for anti-HIV-1 RT activity. The results of in vitro tests showed that the compound 9 (I) exhibited EC50 at 0.26 μM with minimal toxicity in MT-4 cells as compared to 0.35 μM for thiazobenzimidazole (TBZ). It may be inferred from the present data that the majority of compds. in this series exhibit higher selectivity index than TBZ.

SO Bioorganic & Medicinal Chemistry (2007), 15(4), 1725-1731
CODEN: BMECEP; ISSN: 0968-0896

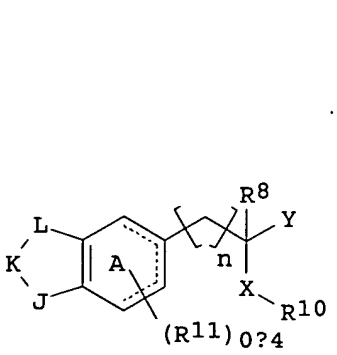
PY 2007

L4 ANSWER 4 OF 184 CAPLUS COPYRIGHT 2007 ACS on STN

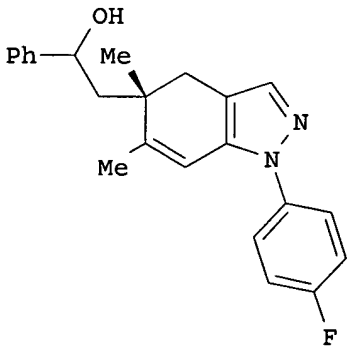
TI Indazole compounds as modulators of glucocorticoid receptor, AP-1, and/or NF-κB activity and their preparation, pharmaceutical compositions and use in the treatment of obesity, diabetes, inflammatory and immune diseases

IN Duan, Jingwu; Lu, Zhonghui; Weinstein, David S.; Jiang, Bin

GI



I



II

AB Non-steroidal compds. are provided which are useful in treating diseases associated with modulation of the glucocorticoid receptor, AP-1, and/or NF-κB activity including obesity, diabetes, inflammatory and immune diseases, and have the structure of formula I or an enantiomer, a diastereomer, a pharmaceutically acceptable salt, or hydrate thereof.

Also provided are pharmaceutical compns. and methods of treating obesity, diabetes and inflammatory or immune associated diseases comprising said compds. Compds. of formula I wherein dotted line is a single and double bond; A is a partially saturated ring; n is 0, 1, and 2; J is (un)substituted alkyl-N, (un)substituted alkenyl-N, (un)substituted methylene, (un)substituted alkynyl-N, etc.; K and L are independently NH and derivs., and (un)substituted methylene; Y is a bond, alkylene, alkenylene, alkynylene, CO< NH and derivs., etc.; Y is H, halo, NO2, CN, OH and derivs., NH2 and derivs., etc.; R8 and R10 are independently H, (un)substituted alkyl, (un)substituted alkenyl, (un)substituted alkynyl, (hetero)aryl, etc.; R11 is (un)substituted alkyl, (un)substituted alkenyl, (un)substituted alkynyl, halo, NO2, azide, CN, OH and derivs., etc,; and their pharmaceutically acceptable salts thereof, are claimed. Example compound II was prepared by condensation of Et 2-methylacetoacetate with (S)-(-)-α-methylbenzylamine; the resulting enamine underwent cyclization with Me vinyl ketone to give Et 1,2-dimethyl-4-oxo-2-cyclohexenecarboxylate, which underwent formylation with Et formate to give the corresponding 6-formyl-2-cyclohexenone, which underwent cyclocondensation with 4-fluorophenylhydrazine to give 5,6-dimethyl-1-(4-fluorophenyl)-4,5-dihydroindazole-5-carboxylic acid Et ester, which underwent reduction to give the corresponding indazole-5-carboxaldehyde, which underwent olefination with (methoxymethyl)triphenylphosphonium chloride to give the corresponding enol ether, which underwent hydrolysis and resolution to give the corresponding (R)-5-indazol-5-ylacetaldehyde, which underwent addition of phenylmagnesium bromide to give followed by resolution to give both the isomers of I. All the invention compds. were evaluated for their glucocorticoid receptor, AP-1 and NF-κB modulatory activity. These compds. may be useful in the treatment of obesity, diabetes, inflammatory and immune disease.

SO PCT Int. Appl., 171pp.
CODEN: PIXXD2

PY 2006

L4 ANSWER 5 OF 184 CAPLUS COPYRIGHT 2007 ACS on STN

TI Synthesis and Antitumor Activity of Guanylhydrazones from 6-(2,4-Dichloro-5-nitrophenyl)imidazo[2,1-b]thiazoles and 6-Pyridylimidazo[2,1-b]thiazoles

AU Andreani, Aldo; Burnelli, Silvia; Granaiola, Massimiliano; Leoni, Alberto; Locatelli, Alessandra; Morigi, Rita; Rambaldi, Mirella; Varoli, Lucilla; Farruggia, Giovanna; Stefanelli, Claudio; Masotti, Lanfranco; Kunkel, Mark W.

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Imidazothiazole guanylhydrazones, e.g., I, were prepared by substitution of bromoketones, e.g., II, with 2-aminothiazoles, e.g., III, followed by Vilsmeier formylation and condensation with aminoguanidine. The antitumor activities of the synthesized guanylhydrazones were tested.

SO Journal of Medicinal Chemistry (2006), 49(26), 7897-7901
CODEN: JMCMAR; ISSN: 0022-2623

PY 2006

L4 ANSWER 6 OF 184 CAPLUS COPYRIGHT 2007 ACS on STN

TI Assessing the Nitrogen and Carbon Nucleophilicities of 2-Aminothiazoles through Coupling with Superelectrophilic 4,6-Dinitrobenzofuroxan

AU Forlani, Luciano; Tocke, Aline Laure; Del Vecchio, Erminia; Lakhdar, Sami; Goumont, Regis; Terrier, Francois

AB The reactions of 2-aminothiazole (1a), 4-methyl-2-aminothiazole (1b), and 4,5-dimethyl-2-aminothiazole (1c) with superelectrophilic

4,6-dinitrobenzofuroxan (DNBF) have been studied in acetonitrile and a 70/30 (volume/volume) H2O/Me2SO mixture While exhibiting a somewhat higher nitrogen basicity than that of anilines, 1a and 1b do not react as nitrogen nucleophiles, affording exclusively anionic C-bonded σ-adducts (C-1a and C-1b) through electrophilic SEAr substitution of the thiazole ring by DNBF. Only in the case of the 4,5-di-Me derivative 1c a N-adduct, N-1c, was obtained. On the basis of 1H-15N correlations, it is demonstrated that this adduct, N-1c;1c,H+, is derived from DNBF addition at the exocyclic amino group and not at the endocyclic nitrogen center of 1c. Rate consts. have been determined in the two solvents for the formation of the adducts, revealing a reactivity sequence which accounts well for the finding that 1a and 1b behave preferentially as carbon rather than nitrogen nucleophiles. The enaminic character of these thiazoles is assessed through an estimation of the pKa values for their C-protonation in aqueous solution as well as through a positioning of their reactivity on the nucleophilicity scale recently developed by Mayr et al. (Acc. Chemical Res. 2003, 36, 66). With N values of the order of 6.80 and 5.56, 1b and 1a have a carbon nucleophilicity comparable to that of N-methylindole and indole, resp.

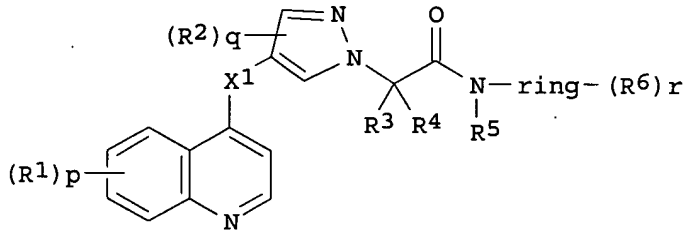
SO Journal of Organic Chemistry (2006), 71(15), 5527-5537
CODEN: JOCEAH; ISSN: 0022-3263
PY 2006

L4 ANSWER 7 OF 184 CAPLUS COPYRIGHT 2007 ACS on STN

TI Preparation of quinoline derivatives for use in treatment of cell proliferative disorders or disease associated with angiogenesis and/or vascular permeability

IN Jung, Frederic Henri

GI



I

AB Quinoline derivs. I, wherein X1 is O, substituted nitrogen; p is 0-3; R1 is halogen, CF3, Cn, OH,SH, NH2, alkyl, alkenyl, alkynyl, alkoxy, alkenyl-oxy, alkynyl-oxy, alkylthio, alkyl-sulfinyl, alkyl-sulfonyl, alkylamino, Q1X2; X2 is O, S, SO, SO2, substituted amine, CO, amide, amino-carbonyl; Q1 is aryl, arylalkyl, cycloalkyl, cyclo-alkenyl, cyclo-alkenyl-alkyl, heteroaryl, heterocycle, heterocyclyl-alkyl; q = 0-2; R2 is halogen CF3, CN, OH, amino, alkyl, alkenyl, alkynyl, alkoxy, alkylamino; R3 is H, alkyl, alkenyl, alkynyl; R3 and R4 together with the carbon atom to which they are attached form a cycloalkyl group; R5 is H, alkyl, alkenyl, alkynyl; ring is 6-membered mono-cyclic, 10-membered bicyclic aryl ring, heterocycle; X1 is O, S, SO, So2, substituted nitrogen, Co, amide, amino-carbonyl, sulfonyl-amine, amino-sulfonyl, ; R6 is halogen, CF3, CN, OH, SH, amino, carboxy, carbamoyl, sulfamoyl, ureido, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkyl-sulfinyl, alkyl-sulfonyl, alkylamino, alkoxycarbonyl, alkanoyl, alkanoyl-oxy, alkyl-carbamoyl; r is 0-3, were prepared for use in the treatment of cell proliferative disorders or in the treatment of disease states associated with angiogenesis and/or vascular permeability. Thus, N-(3-fluorophenyl)-2-[4-(6-cyano-7-methoxy-quinolin-4-yl-oxy)pyrazol-1-yl]acetamide was prepared for use in treatment of cell proliferative disorders or disease associated with angiogenesis and/or vascular permeability. The compds. of the present

invention were tested as inhibitors of PDGFRα, PDGFRβ and KDR tyrosine kinase enzymes, as inhibitors in vitro of the phosphorylation of PDGFR expressed on MG63 osteosarcoma cells, as inhibitors in vitro of the proliferation of MG63 osteosarcoma cells, as inhibitors in vitro of the proliferation of human umbilical vein endothelial cells (HUVECs), and as inhibitors in vivo of the growth in nude mice of xenografts of human tumor tissue such as CaLu-6 and Colo205.

SO PCT Int. Appl., 109 pp.
CODEN: PIXXD2

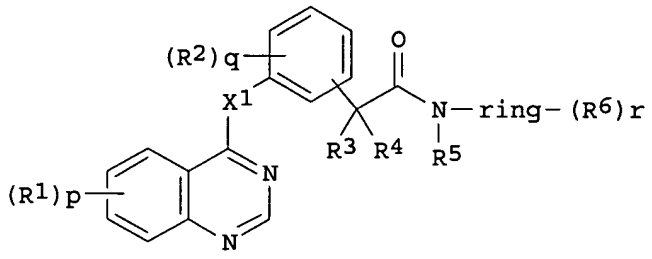
PY 2006

L4 ANSWER 8 OF 184 CAPLUS COPYRIGHT 2007 ACS on STN

TI Preparation of quinazoline derivatives for use in treatment of cell proliferative disorders or disease associated with angiogenesis and/or vascular permeability

IN Ple, Patrick; Jung, Frederic Henri

GI



I

AB Quinazoline derivs. I, wherein X1 is O, substituted amine; p is 0-3; R1 is halogen, CF3, Cn, OH,SH, NH2, alkyl, alkenyl, alkynyl, alkoxy, alkenyl-oxy, alkynyl-oxy, alkylthio, alkyl-sulfinyl, alkyl-sulfonyl, alkylamino, Q1X2; X2 is O, S, SO, SO2, substituted amine, CO, amide, amino-carbonyl; Q1 is aryl, arylalkyl, cycloalkyl, cyclo-alkenyl, cyclo-alkenyl-alkyl, heteroaryl, heterocycle, heterocyclyl-alkyl; q = 0-2; R2 is halogen CF3, CN, OH, amino, alkyl, alkenyl, alkynyl, alkoxy, alkylamino; R3 is H, alkyl, alkenyl, alkynyl; R3 and R4 together with the carbon atom to which they are attached form a cycloalkyl group; R5 is H, alkyl, alkenyl, alkynyl; ring is 6-membered mono-cyclic, 10-membered bicyclic aryl ring, heterocycle; r is 0-3; R6 is halogen, CF3, CN, OH, SH, amino, carboxy, carbamoyl, sulfamoyl, ureido, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkyl-sulfinyl, alkyl-sulfonyl, alkylamino, alkoxycarbonyl, alkanoyl, alkanoyl-oxy, alkyl-carbamoyl, were prepared for use in the treatment of cell proliferative disorders or in the treatment of disease states associated with angiogenesis and/or vascular permeability. Thus, (2S)-2-amino-2-[4-(6,7-dimethoxy-quinazolin-4-yl-oxy)phenyl]-N-(4,5-dimethyl-thiazol-2-yl)acetamide was prepared and tested in treatment of cell proliferative disorders or disease associated with angiogenesis and/or vascular permeability. The compds. of the present invention were tested as inhibitors of PDGFRα, PDGFRβ and KDR tyrosine kinase enzymes, as inhibitors in vitro of the phosphorylation of PDGFR expressed on MG63 osteosarcoma cells, as inhibitors in vitro of the proliferation of MG63 osteosarcoma cells, as inhibitors in vitro of the proliferation of human umbilical vein endothelial cells (HUVECs), and as inhibitors in vivo of the growth in nude mice of xenografts of human tumor tissue such as CaLu-6 and Colo205.

SO PCT Int. Appl., 191 pp.
CODEN: PIXXD2

PY 2006

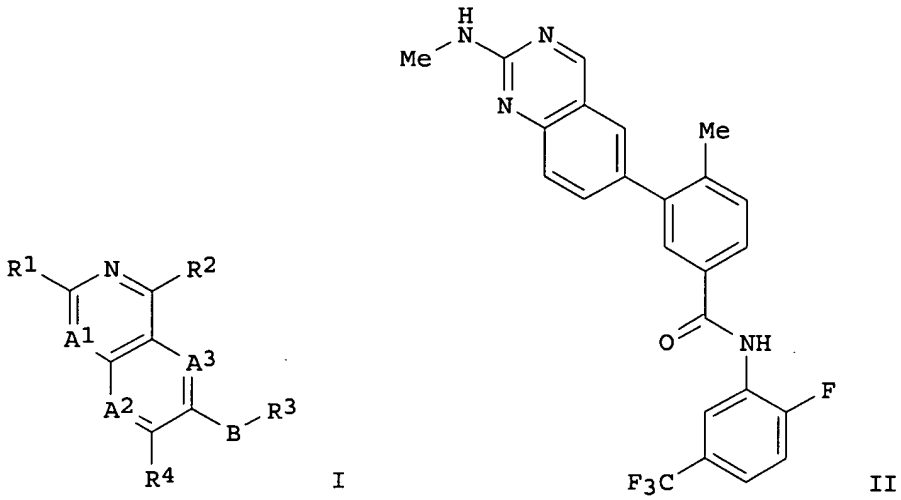
L4 ANSWER 9 OF 184 CAPLUS COPYRIGHT 2007 ACS on STN

TI Aryl nitrogen-containing bicyclic compounds and their preparation,

pharmaceutical compositions, and protein kinase inhibitory activity and use in prophylaxis and treatment of kinase-mediated diseases

IN Patel, Vinod F.; Kim, Joseph L.; Geuns-Meyer, Stephanie D.; Chaffee, Stuart C.; Cee, Victor J.; Hodous, Brian L.; Bellon, Steven; Harmange, Jean-Christophe; Olivieri, Philip R.; Thaman, Maya C.; Dimauro, Erin F.; Buchanan, John L.; Mcgowan, David C.; Albrecht, Brian K.; Deak, Holly L.; Bemis, Jean E.; White, Ryan; Martin, Matthew W.; Habgood, Gregory J.; Tempest, Paul A.; Masse, Craig E.; Buckner, William H.; Herberich, Bradley J.; Graceffa, Russell; Zhang, Dawei; Xu, Shimin; Sham, Kelvin; Rzasa, Robert M.; Falsey, James Richard; Chakrabarti, Partha P.; Cao, Guo-Qiang; Tomlinson, Susan Ann; Pettus, Liping H.; Smith, Adrian Leonard; Paras, Nick A.; Liu, Gang; Demorin, Frenel F.; Tasker, Andrew; Reed, Anthony

GI



AB The invention comprises a class of compds. of formula I useful for the prophylaxis and treatment of protein kinase mediated diseases, including inflammation, cancer and related conditions. Compds. of formula I wherein A1 and one of A2 and A3 are independently CR5 or N; B is a bond, CR5R6, CO, NR6, O, S, SO, or SO2; R1 is halo, haloalkyl, NO2, CN, H, NH2 and derivs., OH and derivs., SH and derivs., CHO and derivs., OC(O)R and derivs., CO2H and derivs., CONH2 and derivs., CSNH2 and derivs., NHCHO and derivs., NHC(S)H and derivs., NHCONH2 and derivs., NHCSNH2 and derivs., SO2H and derivs., SO2NH2 and derivs., etc.; R2, R4, and R5 are independently H, halo, haloalkyl, NO2, CN, OH and derivs., SH and derivs., NH2 and derivs., CHO and derivs., CO2H and derivs., CONH2 and derivs., NHCONH2 and derivs., SO2H and derivs., SO2NH2 and derivs., NHSO2H and derivs., (un)substituted C1-10 (hetero)alkyl, (un)substituted C2-10 alkenyl, (un)substituted C2-10 (hetero)alkynyl, (un)substituted 3- to 10-membered (hetero)cycloalkyl, (un)substituted 4- to 10-membered (hetero)cycloalkenyl, etc.; R3 is (un)substituted (un)saturated 5- to 8-membered (hetero)monocyclic, (un)substituted (un)saturated 6- to 12-membered (hetero)bicyclic, or (un)substituted (un)saturated 7- to 14-membered (hetero)tricyclic rings; R6 is H, (un)substituted C1-10 (hetero)alkyl, (un)substituted C2-10 (hetero)alkenyl, (un)substituted C2-10 (hetero)alkynyl, (un)substituted 3- to 10-membered (hetero)cycloalkyl, (un)substituted 4- to 10-membered (hetero)cycloalkenyl; and their stereoisomers, tautomers, solvates, pharmaceutically acceptable salts, derivs., and prodrugs thereof are claimed. Accordingly, the invention also comprises pharmaceutical compns. comprising the compds. of the invention, methods for the prophylaxis and treatment of kinase mediated

diseases using the compds. and compns. of the invention, and intermediates and processes useful for the preparation of compds. of the invention. Example compound II was prepared by boration of 3-iodo-4-methylbenzoic acid with bis(pinacolato)diboron; the resulting 4-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoic acid was converted to the corresponding acid chloride, in situ, and reacted with 2-fluoro-5-trifluoromethylbenzeneamine to give N-(2-fluoro-5-fluoromethylphenyl)-4-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzamide, which underwent cross-coupling with 6-bromo-N-methylquinazolin-2-amine to give compound II. About 2000 invention compds. of formula I were prepared by similar procedures. All the invention compds. were tested for their protein kinase inhibitory activity. Example compound I along with many other invention compound showed good inhibitory activity. From the HTRF assay, the IC50 values for inhibition of Tie-2 was determined to be less than or equal to 1 μM for some of the invention compds. For the inhibition of Lck kinase enzyme, the some of the exemplary compds. exhibited an average IC50 value of 25 μM or less and some invention compound exhibited an IC50 value of 1 μM or less, in the human HTRF assay. The invention compds. were also found to be active inhibitors or the VEGF kinase receptor. Furthermore, some of the invention compds. exhibited activities in the monocyte assay with IC50 values of 25 μM or less. Various compds. of the invention have selective inhibitory activity for specific kinase receptor enzymes, including Tie-2, Lck, p38 and VEGFR/KDR. Accordingly, the compds. of the invention would be useful in therapy as antineoplasia agents, antiinflammatory agents, or to minimize deleterious effects of Tie-2, Lck, VEGF and/or p38.

SO PCT Int. Appl., 876 pp.
CODEN: PIXXD2

PY 2006
2006
2007

L4 ANSWER 10 OF 184 CAPLUS COPYRIGHT 2007 ACS on STN

TI One pot synthesis using supported reagents system KSCN/SiO2-RNH3OAc/Al2O3: synthesis of 2-aminothiazoles and N-allylthioureas

AU Aoyama, Tadashi; Murata, Sumiko; Arai, Izumi; Araki, Natsumi; Takido, Toshio; Suzuki, Yoshitada; Kodomari, Mitsuo

AB A simple and efficient method has been developed for the synthesis of 2-aminothiazoles and N-allylthioureas from com. available materials in one pot by using a supported reagents system, KSCN/SiO2-RNH3OAc/Al2O3, in which α-halo ketones react first with KSCN/SiO2 and the product, α-thiocyanatoketone, reacts with RNH3OAc/Al2O3 to give the final products, 2-aminothiazoles, in good yield. Allyl bromides react with KSCN/SiO2 and the products, allyl isothiocyanates, react with RNH3OAc/Al2O3 to give N-allylthioureas.

SO Tetrahedron (2006), 62(14), 3201-3213
CODEN: TETRAB; ISSN: 0040-4020

PY 2006

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	30.65	99.91

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-7.80	-7.80

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predicted properties as well as tags indicating availability of
experimental property data in the original document. For information
on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

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E1            1     2-AMINO-4,5-DIMETHYLPYRIMIDINE/CN
E2            1     2-AMINO-4,5-DIMETHYLSELENAZOLE, HYDROCHLORIDE/CN
E3            1 --> 2-AMINO-4,5-DIMETHYLTHIAZOLE/CN
E4            1     2-AMINO-4,5-DIMETHYLTHIAZOLE HYDROBROMIDE/CN
E5            1     2-AMINO-4,5-DIMETHYLTHIAZOLE HYDROCHLORIDE/CN
E6            1     2-AMINO-4,5-DIMETHYLTHIOPHENE-3-CARBOXAMIDE/CN
E7            1     2-AMINO-4,5-DIMETHYLTHIOPHENE-3-CARBOXYLIC ACID/CN
E8            1     2-AMINO-4,5-DINITROPHENOL/CN
E9            1     2-AMINO-4,5-DIPHENYL-1,3-THIAZOLE/CN
E10           1     2-AMINO-4,5-DIPHENYL-3-FURANCARBONITRILE/CN
E11           1     2-AMINO-4,5-DIPHENYLBENZOIC ACID/CN
E12           1     2-AMINO-4,5-DIPHENYLCYCLOPENT-2-ENE-1,1,3-TRICARBONITRILE/CN
E13           1     2-AMINO-4,5-DIPHENYLIMIDAZOLE/CN
E14           1     2-AMINO-4,5-DIPHENYLNICOTINONITRILE/CN
E15           1     2-AMINO-4,5-DIPHENYLOXAZOLE/CN
E16           1     2-AMINO-4,5-DIPHENYLPYRIMIDINE/CN
E17           1     2-AMINO-4,5-DIPHENYLTHIAZOLE/CN
E18           1     2-AMINO-4,5-DIPHENYLTHIAZOLE HYDROCHLORIDE/CN
E19           1     2-AMINO-4,5-IMIDAZOLEDICARBOXYLIC ACID/CN
E20           1     2-AMINO-4,5-METHYLENEDIOXY-A-(4'-METHOXYPHENYL)CINNAMIC ACID/CN
E21           1     2-AMINO-4,5-METHYLENEDIOXY-PHENYLBENZYLMETHANONE/CN
E22           1     2-AMINO-4,5-METHYLENEDIOXYBENZAMIDE/CN
E23           1     2-AMINO-4,5-METHYLENEDIOXYBENZOIC ACID/CN
E24           1     2-AMINO-4,5-METHYLENEDIOXYBENZONITRILE/CN
E25           1     2-AMINO-4,5-PYRIMIDINEDIOL/CN

=> S E3
L5            1 "2-AMINO-4,5-DIMETHYLTHIAZOLE"/CN

=> DIS L5 1 IDE

L5   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2007 ACS on STN
RN   2289-75-0  REGISTRY
ED   Entered STN:  16 Nov 1984
CN   2-Thiazolamine, 4,5-dimethyl- (9CI)  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   Thiazole, 2-amino-4,5-dimethyl- (6CI, 7CI, 8CI)
OTHER NAMES:
CN   2-Amino-4,5-dimethylthiazole
CN   4,5-Dimethyl-2-thiazolamine
MF   C5 H8 N2 S
CI   COM
LC   STN Files:   BEILSTEIN*, CA, CAOLD, CAPLUS, CASREACT, CHEMCATS,
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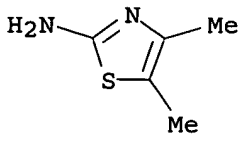
CHEMINFORMRX, CIN, CSCHEM, IFICDB, IFIPAT, IFIUDB, TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

140 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
140 REFERENCES IN FILE CAPLUS (1907 TO DATE)
10 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

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                 (2289-75-0/RN)
      21941271 2
       6775643 AMINO
         11456 AMINOS
       6775643 AMINO
                 (AMINO OR AMINOS)
        619191 4,5
           138 DIMETHYLTHIAZOLE
             3 2-AMINO-4,5-DIMETHYLTHIAZOLE
                 (2(W)AMINO(W)4,5(W)DIMETHYLTHIAZOLE)
L6           3 2289-75-0 OR 2-AMINO-4,5-DIMETHYLTHIAZOLE
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   REGISTRY INITIATED
Substance data SEARCH and crossover from CAS REGISTRY in progress...
Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.

L8          140 L7

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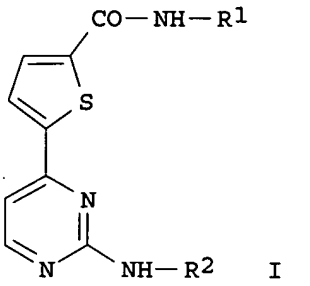
        1112330 AMINO
             44 AMINOS
        1112348 AMINO
                   (AMINO OR AMINOS)
        5555409 4
        6355474 5
            798 DIMETHYLTHIAZOLE
             16 DIMETHYLTHIAZOLES
            808 DIMETHYLTHIAZOLE
                   (DIMETHYLTHIAZOLE OR DIMETHYLTHIAZOLES)
             97 2-AMINO-4,5-DIMETHYLTHIAZOLE
                   (2(W)AMINO(W)4(W)5(W)DIMETHYLTHIAZOLE)
L9          172 L8 OR 2-AMINO-4,5-DIMETHYLTHIAZOLE


=> d ti au abs so py 1-10

L9   ANSWER 1 OF 172  CAPLUS  COPYRIGHT 2007 ACS on STN
TI   Preparation of pyrimidyl-thiophene derivatives as Aurora kinase inhibitors
IN   Adams, Jerry Leroy; Drewry, David Harold; Linn, James Andrew
GI
```



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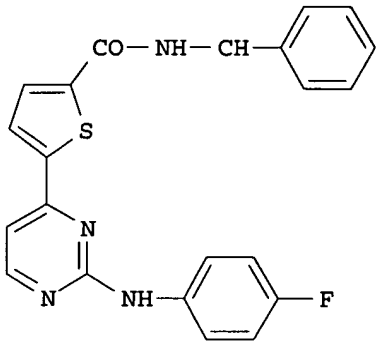


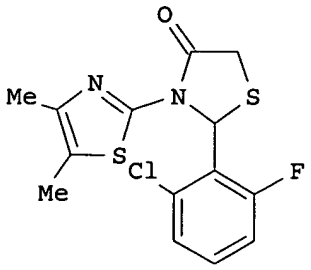
II

AB Title compds. I [R1 = HO(CH2)4-, NCCH2-, (un)substituted Ph, phenylalkyl, etc.; R2 = 2-(N,N-dimethylaminoethyl)-1,3-dioxo-2H-isoindol-5-yl, 2-(N,N-dimethylaminomethyl)-benzoxazol-6-yl, or substituted phenyl], and their pharmaceutically acceptable salts, are prepared and disclosed as Aurora kinase inhibitors. Thus, e.g., II was prepared by cyclocondensation of 5-[(2E)-3-(dimethylamino)-2-propenoyl]-N-(phenylmethyl)-2-thiophenecaboxamide (preparation given) with 1-(4-fluorophenyl)guanidine carbonate. I were tested for their Aurora kinase inhibitory activity and demonstrated pIC50 values ≥ 5.0. I as inhibitors of Aurora kinase activity should prove useful for the treatment and prevention of diseases associated with cell proliferation such as cancer.
SO PCT Int. Appl., 205pp.
CODEN: PIXXD2
PY 2007

L9 ANSWER 2 OF 172 CAPLUS COPYRIGHT 2007 ACS on STN
TI 2-Amino-5-aminomethylphenol derivatives for dyeing hair fibers
IN Pasquier, Cecile; Tinguely, Eric; Buclin, Veronique; Braun, Hans-Juergen
AB The object of the present patent application are new 2-amino-5-aminomethylphenol derivs. and colorants for oxidative dyeing of keratin fibers, particularly human hair, containing at least 1 2-amino-5-aminomethyl-phenol derivative or a water-soluble salt thereof. A 2-amino-5-aminomethylphenol derivative was prepared and used 0.00125 mol along with a developer in a hair dye formulation.
SO Eur. Pat. Appl., 28pp.
CODEN: EPXXDW
PY 2007
2007
2007

L9 ANSWER 3 OF 172 CAPLUS COPYRIGHT 2007 ACS on STN
TI Design, synthesis, and evaluation of 2-aryl-3-heteroaryl-1,3-thiazolidin-4-ones as anti-HIV agents
AU Rawal, Ravindra K.; Tripathi, Rajkamal; Katti, S. B.; Pannecouque, Christophe; De Clercq, Erik

GI



I

AB Compds. having isothiourea or thiourea functional group have shown high anti-HIV-1 activity. Therefore, a series of 2-aryl-3-heteroaryl-1,3-thiazolidin-4-ones were designed, synthesized, and evaluated for anti-HIV-1 RT activity. The results of in vitro tests showed that the compound 9 (I) exhibited EC50 at 0.26 μM with minimal toxicity in MT-4 cells as compared to 0.35 μM for thiazobenzimidazole (TBZ). It may be inferred from the present data that the majority of compds. in this series exhibit higher selectivity index than TBZ.

SO Bioorganic & Medicinal Chemistry (2007), 15(4), 1725-1731
CODEN: BMECEP; ISSN: 0968-0896

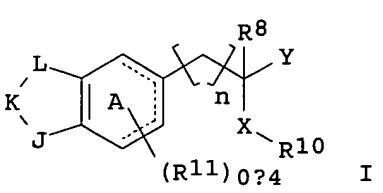
PY 2007

L9 ANSWER 4 OF 172 CAPLUS COPYRIGHT 2007 ACS on STN

TI Indazole compounds as modulators of glucocorticoid receptor, AP-1, and/or NF-κB activity and their preparation, pharmaceutical compositions and use in the treatment of obesity, diabetes, inflammatory and immune diseases

IN Duan, Jingwu; Lu, Zhonghui; Weinstein, David S.; Jiang, Bin

GI



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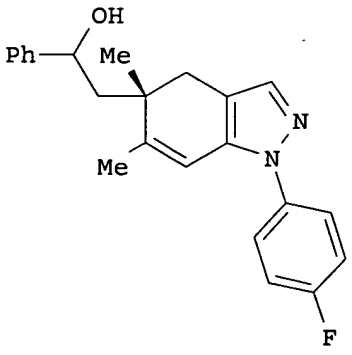


II

AB Non-steroidal compds. are provided which are useful in treating diseases associated with modulation of the glucocorticoid receptor, AP-1, and/or NF-κB activity including obesity, diabetes, inflammatory and immune diseases, and have the structure of formula I or an enantiomer, a diastereomer, a pharmaceutically acceptable salt, or hydrate thereof.

Also provided are pharmaceutical compns. and methods of treating obesity, diabetes and inflammatory or immune associated diseases comprising said compds. Compds. of formula I wherein dotted line is a single and double bond; A is a partially saturated ring; n is 0, 1, and 2; J is (un)substituted alkyl-N, (un)substituted alkenyl-N, (un)substituted methylene, (un)substituted alkynyl-N, etc.; K and L are independently NH and derivs., and (un)substituted methylene; Y is a bond, alkylene, alkenylene, alkynylene, CO< NH and derivs., etc.; Y is H, halo, NO2, CN, OH and derivs., NH2 and derivs., etc.; R8 and R10 are independently H, (un)substituted alkyl, (un)substituted alkenyl, (un)substituted alkynyl, (hetero)aryl, etc.; R11 is (un)substituted alkyl, (un)substituted alkenyl, (un)substituted alkynyl, halo, NO2, azide, CN, OH and derivs., etc,; and their pharmaceutically acceptable salts thereof, are claimed. Example compound II was prepared by condensation of Et 2-methylacetoacetate with (S)-(-)-α-methylbenzylamine; the resulting enamine underwent cyclization with Me vinyl ketone to give Et 1,2-dimethyl-4-oxo-2-cyclohexenecarboxylate, which underwent formylation with Et formate to give the corresponding 6-formyl-2-cyclohexenone, which underwent cyclocondensation with 4-fluorophenylhydrazine to give 5,6-dimethyl-1-(4-fluorophenyl)-4,5-dihydroindazole-5-carboxylic acid Et ester, which underwent reduction to give the corresponding indazole-5-carboxaldehyde, which underwent olefination with (methoxymethyl)triphenylphosphonium chloride to give the corresponding enol ether, which underwent hydrolysis and resolution to give the corresponding (R)-5-indazol-5-ylacetaldehyde, which underwent addition of phenylmagnesium bromide to give followed by resolution to give both the isomers of I. All the invention compds. were evaluated for their glucocorticoid receptor, AP-1 and NF-κB modulatory activity. These compds. may be useful in the treatment of obesity, diabetes, inflammatory and immune disease.

SO PCT Int. Appl., 171pp.
CODEN: PIXXD2

PY 2006

L9 ANSWER 5 OF 172 CAPLUS COPYRIGHT 2007 ACS on STN

TI Synthesis and Antitumor Activity of Guanylhydrazones from 6-(2,4-Dichloro-5-nitrophenyl)imidazo[2,1-b]thiazoles and 6-Pyridylimidazo[2,1-b]thiazoles

AU Andreani, Aldo; Burnelli, Silvia; Granaiola, Massimiliano; Leoni, Alberto; Locatelli, Alessandra; Morigi, Rita; Rambaldi, Mirella; Varoli, Lucilla; Farruggia, Giovanna; Stefanelli, Claudio; Masotti, Lanfranco; Kunkel, Mark W.

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Imidazothiazole guanylhydrazones, e.g., I, were prepared by substitution of bromoketones, e.g., II, with 2-aminothiazoles, e.g., III, followed by Vilsmeier formylation and condensation with aminoguanidine. The antitumor activities of the synthesized guanylhydrazones were tested.

SO Journal of Medicinal Chemistry (2006), 49(26), 7897-7901
CODEN: JMCMAR; ISSN: 0022-2623

PY 2006

L9 ANSWER 6 OF 172 CAPLUS COPYRIGHT 2007 ACS on STN

TI Assessing the Nitrogen and Carbon Nucleophilicities of 2-Aminothiazoles through Coupling with Superelectrophilic 4,6-Dinitrobenzofuroxan

AU Forlani, Luciano; Tocke, Aline Laure; Del Vecchio, Erminia; Lakhdar, Sami; Goumont, Regis; Terrier, Francois

AB The reactions of 2-aminothiazole (1a), 4-methyl-2-aminothiazole (1b), and 4,5-dimethyl-2-aminothiazole (1c) with superelectrophilic

4,6-dinitrobenzofuroxan (DNBF) have been studied in acetonitrile and a 70/30 (volume/volume) H2O/Me2SO mixture While exhibiting a somewhat higher nitrogen basicity than that of anilines, 1a and 1b do not react as nitrogen nucleophiles, affording exclusively anionic C-bonded σ-adducts (C-1a and C-1b) through electrophilic SEAr substitution of the thiazole ring by DNBF. Only in the case of the 4,5-di-Me derivative 1c a N-adduct, N-1c, was obtained. On the basis of 1H-15N correlations, it is demonstrated that this adduct, N-1c;1c,H+, is derived from DNBF addition at the exocyclic amino group and not at the endocyclic nitrogen center of 1c. Rate consts. have been determined in the two solvents for the formation of the adducts, revealing a reactivity sequence which accounts well for the finding that 1a and 1b behave preferentially as carbon rather than nitrogen nucleophiles. The enaminic character of these thiazoles is assessed through an estimation of the pKa values for their C-protonation in aqueous solution as well as through a positioning of their reactivity on the nucleophilicity scale recently developed by Mayr et al. (Acc. Chemical Res. 2003, 36, 66). With N values of the order of 6.80 and 5.56, 1b and 1a have a carbon nucleophilicity comparable to that of N-methylindole and indole, resp.

SO Journal of Organic Chemistry (2006), 71(15), 5527-5537
CODEN: JOCEAH; ISSN: 0022-3263

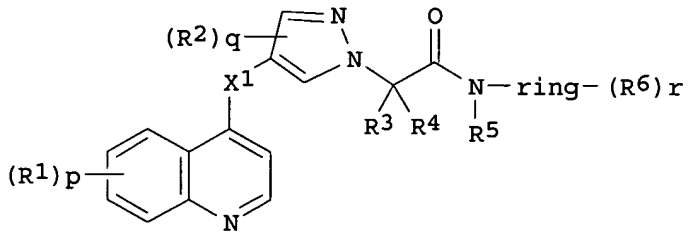
PY 2006

L9 ANSWER 7 OF 172 CAPLUS COPYRIGHT 2007 ACS on STN

TI Preparation of quinoline derivatives for use in treatment of cell proliferative disorders or disease associated with angiogenesis and/or vascular permeability

IN Jung, Frederic Henri

GI



I

AB Quinoline derivs. I, wherein X1 is O, substituted nitrogen; p is 0-3; R1 is halogen, CF3, Cn, OH,SH, NH2, alkyl, alkenyl, alkynyl, alkoxy, alkenyl-oxy, alkynyl-oxy, alkylthio, alkyl-sulfinyl, alkyl-sulfonyl, alkylamino, Q1X2; X2 is O, S, SO, SO2, substituted amine, CO, amide, amino-carbonyl; Q1 is aryl, arylalkyl, cycloalkyl, cyclo-alkenyl, cyclo-alkenyl-alkyl, heteroaryl, heterocycle, heterocyclyl-alkyl; q = 0-2; R2 is halogen CF3, CN, OH, amino, alkyl, alkenyl, alkynyl, alkoxy, alkylamino; R3 is H, alkyl, alkenyl, alkynyl; R3 and R4 together with the carbon atom to which they are attached form a cycloalkyl group; R5 is H, alkyl, alkenyl, alkynyl; ring is 6-membered mono-cyclic, 10-membered bicyclic aryl ring, heterocycle; X1 is O, S, SO, So2, substituted nitrogen, Co, amide, amino-carbonyl, sulfonyl-amine, amino-sulfonyl, ; R6 is halogen, CF3, CN, OH, SH, amino, carboxy, carbamoyl, sulfamoyl, ureido, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkyl-sulfinyl, alkyl-sulfonyl, alkylamino, alkoxycarbonyl, alkanoyl, alkanoyl-oxy, alkyl-carbamoyl; r is 0-3, were prepared for use in the treatment of cell proliferative disorders or in the treatment of disease states associated with angiogenesis and/or vascular permeability. Thus, N-(3-fluorophenyl)-2-[4-(6-cyano-7-methoxy-quinolin-4-yl-oxy)pyrazol-1-yl]acetamide was prepared for use in treatment of cell proliferative disorders or disease associated with angiogenesis and/or vascular permeability. The compds. of the present

invention were tested as inhibitors of PDGFRα, PDGFRβ and KDR tyrosine kinase enzymes, as inhibitors in vitro of the phosphorylation of PDGFR expressed on MG63 osteosarcoma cells, as inhibitors in vitro of the proliferation of MG63 osteosarcoma cells, as inhibitors in vitro of the proliferation of human umbilical vein endothelial cells (HUVECs), and as inhibitors in vivo of the growth in nude mice of xenografts of human tumor tissue such as CaLu-6 and Colo205.

SO PCT Int. Appl., 109 pp.
CODEN: PIXXD2

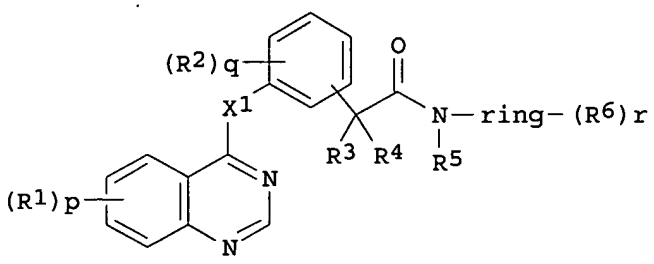
PY 2006

L9 ANSWER 8 OF 172 CAPLUS COPYRIGHT 2007 ACS on STN

TI Preparation of quinazoline derivatives for use in treatment of cell proliferative disorders or disease associated with angiogenesis and/or vascular permeability

IN Ple, Patrick; Jung, Frederic Henri

GI



I

AB Quinazoline derivs. I, wherein X1 is O, substituted amine; p is 0-3; R1 is halogen, CF3, Cn, OH,SH, NH2, alkyl, alkenyl, alkynyl, alkoxy, alkenyl-oxy, alkynyl-oxy, alkylthio, alkyl-sulfinyl, alkyl-sulfonyl, alkylamino, Q1X2; X2 is O, S, SO, SO2, substituted amine, CO, amide, amino-carbonyl; Q1 is aryl, arylalkyl, cycloalkyl, cyclo-alkenyl, cyclo-alkenyl-alkyl, heteroaryl, heterocycle, heterocyclyl-alkyl; q = 0-2; R2 is halogen CF3, CN, OH, amino, alkyl, alkenyl, alkynyl, alkoxy, alkylamino; R3 is H, alkyl, alkenyl, alkynyl; R3 and R4 together with the carbon atom to which they are attached form a cycloalkyl group; R5 is H, alkyl, alkenyl, alkynyl; ring is 6-membered mono-cyclic, 10-membered bicyclic aryl ring, heterocycle; r is 0-3; R6 is halogen, CF3, CN, OH, SH, amino, carboxy, carbamoyl, sulfamoyl, ureido, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkyl-sulfinyl, alkyl-sulfonyl, alkylamino, alkoxycarbonyl, alkanoyl, alkanoyl-oxy, alkyl-carbamoyl, were prepared for use in the treatment of cell proliferative disorders or in the treatment of disease states associated with angiogenesis and/or vascular permeability. Thus, (2S)-2-amino-2-[4-(6,7-dimethoxy-quinazolin-4-yl-oxy)phenyl]-N-(4,5-dimethyl-thiazol-2-yl)acetamide was prepared and tested in treatment of cell proliferative disorders or disease associated with angiogenesis and/or vascular permeability. The compds. of the present invention were tested as inhibitors of PDGFRα, PDGFRβ and KDR tyrosine kinase enzymes, as inhibitors in vitro of the phosphorylation of PDGFR expressed on MG63 osteosarcoma cells, as inhibitors in vitro of the proliferation of MG63 osteosarcoma cells, as inhibitors in vitro of the proliferation of human umbilical vein endothelial cells (HUVECs), and as inhibitors in vivo of the growth in nude mice of xenografts of human tumor tissue such as CaLu-6 and Colo205.

SO PCT Int. Appl., 191 pp.
CODEN: PIXXD2

PY 2006

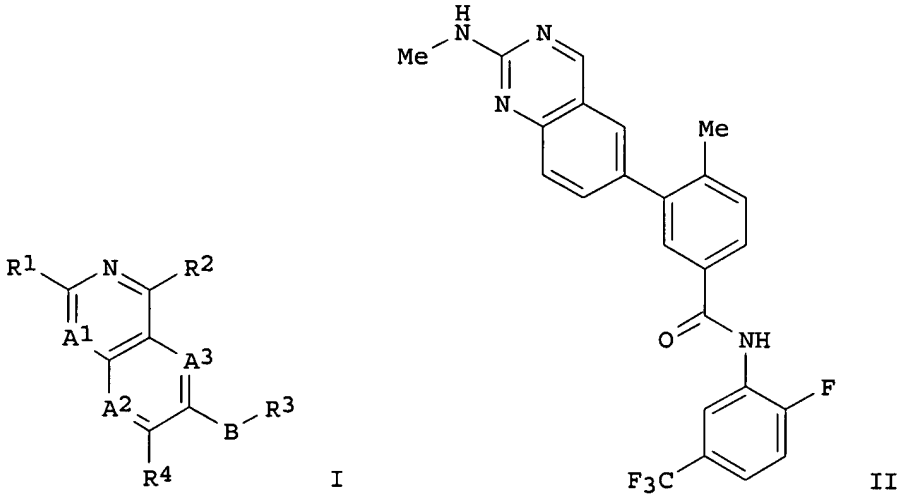
L9 ANSWER 9 OF 172 CAPLUS COPYRIGHT 2007 ACS on STN

TI Aryl nitrogen-containing bicyclic compounds and their preparation,

pharmaceutical compositions, and protein kinase inhibitory activity and use in prophylaxis and treatment of kinase-mediated diseases

IN Patel, Vinod F.; Kim, Joseph L.; Geuns-Meyer, Stephanie D.; Chaffee, Stuart C.; Cee, Victor J.; Hodous, Brian L.; Bellon, Steven; Harmange, Jean-Christophe; Olivieri, Philip R.; Thaman, Maya C.; Dimauro, Erin F.; Buchanan, John L.; Mcgowan, David C.; Albrecht, Brian K.; Deak, Holly L.; Bemis, Jean E.; White, Ryan; Martin, Matthew W.; Habgood, Gregory J.; Tempest, Paul A.; Masse, Craig E.; Buckner, William H.; Herberich, Bradley J.; Graceffa, Russell; Zhang, Dawei; Xu, Shimin; Sham, Kelvin; Rzasa, Robert M.; Falsey, James Richard; Chakrabarti, Partha P.; Cao, Guo-Qiang; Tomlinson, Susan Ann; Pettus, Liping H.; Smith, Adrian Leonard; Paras, Nick A.; Liu, Gang; Demorin, Frenel F.; Tasker, Andrew; Reed, Anthony

GI



AB The invention comprises a class of compds. of formula I useful for the prophylaxis and treatment of protein kinase mediated diseases, including inflammation, cancer and related conditions. Compds. of formula I wherein A1 and one of A2 and A3 are independently CR5 or N; B is a bond, CR5R6, CO, NR6, O, S, SO, or SO2; R1 is halo, haloalkyl, NO2, CN, H, NH2 and derivs., OH and derivs., SH and derivs., CHO and derivs., OC(O)R and derivs., CO2H and derivs., CONH2 and derivs., CSNH2 and derivs., NHCHO and derivs., NHC(S)H and derivs., NHCONH2 and derivs., NHCSNH2 and derivs., SO2H and derivs., SO2NH2 and derivs., etc.; R2, R4, and R5 are independently H, halo, haloalkyl, NO2, CN, OH and derivs., SH and derivs., NH2 and derivs., CHO and derivs., CO2H and derivs., CONH2 and derivs., NHCONH2 and derivs., SO2H and derivs., SO2NH2 and derivs., NHSO2H and derivs., (un)substituted C1-10 (hetero)alkyl, (un)substituted C2-10 alkenyl, (un)substituted C2-10 (hetero)alkynyl, (un)substituted 3- to 10-membered (hetero)cycloalkyl, (un)substituted 4- to 10-membered (hetero)cycloalkenyl, etc.; R3 is (un)substituted (un)saturated 5- to 8-membered (hetero)monocyclic, (un)substituted (un)saturated 6- to 12-membered (hetero)bicyclic, or (un)substituted (un)saturated 7- to 14-membered (hetero)tricyclic rings; R6 is H, (un)substituted C1-10 (hetero)alkyl, (un)substituted C2-10 (hetero)alkenyl, (un)substituted C2-10 (hetero)alkynyl, (un)substituted 3- to 10-membered (hetero)cycloalkyl, (un)substituted 4- to 10-membered (hetero)cycloalkenyl; and their stereoisomers, tautomers, solvates, pharmaceutically acceptable salts, derivs., and prodrugs thereof are claimed. Accordingly, the invention also comprises pharmaceutical compns. comprising the compds. of the invention, methods for the prophylaxis and treatment of kinase mediated

diseases using the compds. and compns. of the invention, and intermediates and processes useful for the preparation of compds. of the invention. Example compound II was prepared by boration of 3-iodo-4-methylbenzoic acid with bis(pinacolato)diboron; the resulting 4-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzoic acid was converted to the corresponding acid chloride, in situ, and reacted with 2-fluoro-5-trifluoromethylbenzeneamine to give N-(2-fluoro-5-fluoromethylphenyl)-4-methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzamide, which underwent cross-coupling with 6-bromo-N-methylquinazolin-2-amine to give compound II. About 2000 invention compds. of formula I were prepared by similar procedures. All the invention compds. were tested for their protein kinase inhibitory activity. Example compound I along with many other invention compound showed good inhibitory activity. From the HTRF assay, the IC50 values for inhibition of Tie-2 was determined to be less than or equal to 1 μM for some of the invention compds. For the inhibition of Lck kinase enzyme, the some of the exemplary compds. exhibited an average IC50 value of 25 μM or less and some invention compound exhibited an IC50 value of 1 μM or less, in the human HTRF assay. The invention compds. were also found to be active inhibitors or the VEGF kinase receptor. Furthermore, some of the invention compds. exhibited activities in the monocyte assay with IC50 values of 25 μM or less. Various compds. of the invention have selective inhibitory activity for specific kinase receptor enzymes, including Tie-2, Lck, p38 and VEGFR/KDR. Accordingly, the compds. of the invention would be useful in therapy as antineoplasia agents, antiinflammatory agents, or to minimize deleterious effects of Tie-2, Lck, VEGF and/or p38.

SO PCT Int. Appl., 876 pp.
CODEN: PIXXD2

PY 2006.
2006
2007

L9 ANSWER 10 OF 172 CAPLUS COPYRIGHT 2007 ACS on STN

TI One pot synthesis using supported reagents system KSCN/SiO2-RNH3OAc/Al2O3: synthesis of 2-aminothiazoles and N-allylthioureas

AU Aoyama, Tadashi; Murata, Sumiko; Arai, Izumi; Araki, Natsumi; Takido, Toshio; Suzuki, Yoshitada; Kodomari, Mitsuo

AB A simple and efficient method has been developed for the synthesis of 2-aminothiazoles and N-allylthioureas from com. available materials in one pot by using a supported reagents system, KSCN/SiO2-RNH3OAc/Al2O3, in which α-halo ketones react first with KSCN/SiO2 and the product, α-thiocyanatoketone, reacts with RNH3OAc/Al2O3 to give the final products, 2-aminothiazoles, in good yield. Allyl bromides react with KSCN/SiO2 and the products, allyl isothiocyanates, react with RNH3OAc/Al2O3 to give N-allylthioureas.

SO Tetrahedron (2006), 62(14), 3201-3213
CODEN: TETRAB; ISSN: 0040-4020

PY 2006

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